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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/381,598	Applicant(s) MIHARA, MASAHIKO
	Examiner Fozia Hamud	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Sep 20, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-13* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-13* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-13 are pending and under consideration by the Examiner.

2. Drawings have been approved by the draftsman

Specification

3. It is noted that this application appears to claim subject matter disclosed in prior PCT Application No. PCT/JP98/01217, filed on 03/20/98, now WO 98/42377. A reference to the prior application must be inserted as the first sentence of the specification of this application if Applicant intends to rely on the filing date of the prior application under 35 U.S.C. 120. See 37 CFR 1.78(a). It is suggested that below the title of the invention be inserted:

Cross Reference to Related Applications

"This Application is a 371 of WO 98/42377".

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridoma cell lines producing the PM-1 and the MR16-1 monoclonal antibodies are required to practice the claimed invention. As such the PM-1 and MR16-1 hybridoma

cell lines must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If the PM-1 and MR16-1 hybridoma cell lines are not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of said hybridoma cell lines.

The specification lacks deposit information for the deposit of the hybridoma cell lines producing the claimed PM-1 and MR16-1 monoclonal antibodies. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, © the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

3b. Claims 1-13, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific monoclonal anti-human IL-6 receptor antibody (PM-1) recited

in claim 9 and the specific monoclonal anti-mouse IL-6 receptor antibody (MR16-1) recited in claim 7, and a method of treating delayed foot pad edema comprising administering said antibodies, does not reasonably provide enablement for a "preventive" agent, or for "all possible" agents comprising IL-6 antagonists as active ingredients, or any agent that prevents or treats multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-13 recite " a preventative or therapeutic agent...", however, the instant specification does not disclose one single agent that is a "preventive" agent, it has no Examples where a disease has been prevented by the claimed agent. Therefore, the instant specification is non-enabling for a preventative agent. With respect to claim 1 which recites "a preventive or therapeutic agent....comprising an IL-6 antagonist as an active ingredient", what is claimed in the instant invention is all therapeutic agents which comprise IL-6 antagonists as active ingredients, however, the specification discloses only two anti-IL-6 receptor monoclonal antibodies, PM-1 and MR16-1 both of which have been shown to have IL-6 antagonistic activities, (see page 32 line 31 through page 35 line 26). The instant specification shows that PM-1 antibody inhibits the binding of IL-6 to IL-6 receptor, (see page 34, lines 14-16). The specification also demonstrates that MR16-1 monoclonal antibody suppresses IL-6 induced incorporation of ^{3}H-thymidine of MH60.BSF2 cells and that it also inhibits the binding of IL-6 to IL-6 receptor, (page 35, lines 22-26). The instant specification also discloses that one time administration of the MR16-1 monoclonal antibody inhibits the delayed foot pad edema reaction caused by injection of mycobacterium butyricum to the right foot of C57BL/6 mice, (see page 29, line 24 through page 30, line 9 and figure 1). Thus the instant

specification is only enabling for the specific monoclonal MR16-1 and PM-1 antibodies, said antibodies having specific characteristics and properties. These properties differ structurally, chemically and physically from other known agents which have IL-6 antagonists as active ingredients. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, in the instant application, the quantity of experimentation to perform in order to determine all the therapeutic agents which comprise IL-6 antagonists as active ingredients, as encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine which therapeutic agents comprising IL-6 antagonists as active ingredient having the desired biological activities, would be encompassed by the scope of the claims.

With respect to claim 11, which is drawn to a preventive or therapeutic agent for multiple sclerosis, the instant specification is non-enabling for any agent that prevents or treats multiple sclerosis, Applicant does not present any Examples of a preventative or therapeutic agent that prevents or treats multiple sclerosis. Instant specification merely mentions that the claimed anti-IL-6 receptor antibodies may be useful as therapeutic agents for multiple sclerosis, (page 35, lines 29-35). Multiple sclerosis is a demyelinating disorder of the central nervous system with many disparate clinical manifestations, with no known cure or treatment to date. There is no guidance and working

examples in the specification regarding an agent that treats or prevents multiple sclerosis, therefore, the mere mention that the claimed antibodies may be useful as therapeutic agents for multiple sclerosis, is insufficient support for the claims reciting a preventive or therapeutic agent for multiple sclerosis.

Thus, Applicants are only enabling for the specific anti-IL-6 receptor monoclonal antibodies (PM-1 and MR16-1) as therapeutic agents for diseases involving IL-6.

Claims 6, 7 and 10 are rejected as under 35 U.S.C. 112, first paragraph, so far as they depend on claim 1 for limitation.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 1, are vague and indefinite for the recitation of "a preventive or therapeutic agent for sensitized T cell-mediated disease...." because, it is unclear which diseases are sensitized T cell-mediated diseases. Appropriate correction is required.

Claims 2-11 are rejected as being vague and indefinite insofar as they depend on claim 1 for the "sensitized T cell-mediated disease..." limitation.

Claim rejections-Double patenting

Statutory double patenting rejection

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See Miller v. Eagle Mfg. Co., 151 U.S. 186 (1894); In re Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5a. Claims 2-4, 6, 8-9 and 13 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3 and 6 of prior U.S. Patent No. 5,670,373. This is a double patenting rejection.

Non-statutory double patenting rejection (obviousness-type)

5b. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5c. Claims 1, 10-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,670,373. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1 and 12 of the instant Application are drawn to an agent comprising an IL-6 antagonist as an active ingredient. Claim 1 of 5,670,373 (having the same assignee with the instant application) is drawn to an isolated antibody to human IL-6 receptor wherein the antibody specifically binds to said human IL-6 receptor. The antibody against IL-6 receptor disclosed in the U.S Patent 5,670,373, antagonizes the action of IL-6 because it inhibits the binding of IL-6 to IL-6 receptor, and suppresses IL-6 induced incorporation of ^{3}H-thymidine by KT3 cells (IL-6 dependent human T-cell leukemia line), (column 6, lines 50-65 and figure 5). Furthermore, it would be obvious to one of ordinary skill in the art to humanize the monoclonal antibody disclosed in the 5,670,373 patent , because humanized antibodies are less immunogenic in humans while retaining their therapeutic effects, (Queen et al, U.S Patent 5,530,101). The patented claims are obvious from the instant claims because the instant claims are directed to genus subject matter in which the patented claims are one specific embodiment. The patented product is included in the instant claims. The patent claims if infringed upon would also result in infringement of the broad claims of the instant Application. Allowance of the pending claims, therefore, would have the effect of extending the enforceable life of the allowed claims beyond statutory limit.

ASSIGNEE REQUIRED TO NAME PRIOR INVENTOR?

6. Claims 2, 3, 4, 8, 9 and 13 are directed to the same invention as that of claim 1 of the commonly assigned U.S Patent 5,670,373, and claims 6, 9 are directed to the same invention of claim 6 of commonly assigned 5,670,373. The issue of priority under 35 U.S.C. 102(g) and possibly 35 U.S.C. 102(f) of this single invention must be resolved.

Since the Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the assignee is required to state which entity is the prior inventor of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of monopoly.

Failure to comply with this requirement will result in a holding of abandonment of this application.

Claim rejections-35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> *(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.*

7a. Claims 1-4, 6, 8-13 are rejected under 35 U.S.C *§ 102*(e) as being anticipated by Tadamitsu Kishimoto (U.S. Patent No. 5,670,373).

Kishimoto teaches a humanized monoclonal antibody specific for IL-6 receptor, (see abstract and column 2, lines 11-39). The monoclonal antibody disclosed by Kishimoto was named PM1 and was shown to specifically bind to IL-6 receptor (column 4, line 45 through column 5 line 41). The PM1 monoclonal antibody disclosed by Kishimoto, inhibits the binding of IL-6 to IL-6 receptor, and suppresses IL-6 induced incorporation of ^{3}H-thymidine by KT3 cells (IL-6 dependent human T-cell leukemia line), (column 6, lines 50-65 and figure 5).

Claims 1-4, 6, 8-13 of the instant invention are drawn to a therapeutic agent comprising an IL-6 antagonist as an active ingredient, wherein said agent is a monoclonal antibody and wherein said monoclonal antibody is PM-1 antibody.

Therefore the Kishimoto reference clearly anticipates claims 1-4, 6, 8-13 of the instant Application.

Claim rejections-35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action: Application.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8a. Claims 1-4, 5, 7-13 are rejected under 35 U.S.C *§ 102*(b) as being anticipated by Kishimoto et al (WO 96/11020).

Kishimoto et al teach a mouse monoclonal antibody specific for IL-6 receptor, said monoclonal antibody was named MR16-1 and was shown to specifically bind to IL-6 receptor

and inhibit IL-6 induced uptake of ^{3}H-thymidine by MH60.BSF2 cells (see page 20, line 5 through page 21 line 14).

Claims 1-4, 5, 7-13 of the instant invention are drawn to a therapeutic agent comprising an IL-6 antagonist as an active ingredient, wherein said agent is a mouse monoclonal antibody and wherein said monoclonal antibody is MR16-1 antibody.

Therefore the Kishimoto reference clearly anticipates claims 1-4, 5, 7-13 of the instant Application.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8896. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1646
April 04, 2000

Prema Mertz

PREMA MERTZ
PRIMARY EXAMINER